James Heard

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Eleven Editions of Osler

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James D. Heard, M. D.,
121 University Place,
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Dear Doctor Heard -

For your gracious letter of September 21st, I want to thank you most sincerely. A few such letters as this would apoil me entirely. Nevertheless, I am grateful to you for your courtesy in taking the time to write as you did, and your letter is all the more welcome because it comes from one so closely associated with Osler.

Some time at one of the meetings of the National Association, or perhaps in connection with other meetings, I hope we will have the pleasure of meeting each other. I will be very glad indeed to have the opportunity to meet you and thank you personally for your letter.

With kindest regards,

Sincerely yours,

James G. Carr

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ELEVEN EDITIONS OF OSLER

By James G. Carr, M.D., Chicago

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IT is with some wistfulness that I recall my first acquaintance with Osler's *Text Book of the Principles and Practice of Medicine.* Though my memory of the conversation is hazy, there remains a vivid impression of the enthusiasm of my father as he spoke of this relatively young man who was then taking up work at the new school, Johns Hopkins, in Baltimore. I did sense my father's feeling that the author had already shown himself a man of unusual promise and that his book might mark a new era in medicine. Within a few years these expectations were amply fulfilled; Osler did become a Master in Medicine and his Text Book a milestone in the progress of medical knowledge.

That evening's conversation was carried on in the light of an oil lamp, in a home that faced an unpaved street. At that time of the year, if the ground was not frozen, the street must have been deep with mud, through which three or four horses took turns, single or double, in carrying the doctor on his rounds. How well, too, is the old office remembered, the grate fire in the uncarpeted waiting room, the long shelves of medicines which almost filled the room devoted to consultation purposes; the back room with the five-quart bottles of medicine ready for dispensing, and the inevitable skeleton in the closet. Before the days of the x-ray, the general practitioner was likely to possess a skeleton; it was of service when studying the care of fractures.

The contrast between the living conditions of then and now is striking enough but these changes seem small indeed when compared with the almost wholly altered methods of medical practice which have been developed since Osler's first edition appeared. There was a small microscope in that office, used almost solely for examining urinary sediments, but no instrument for counting blood corpuscles, none for determining blood pressure. Blood for examination was never drawn from a vein; no needle was at hand for spinal puncture; the possibility of determining by culture of the blood the type of an infectious disease had been conceived, but in no sense of the word was it a diagnostic procedure. There was no discussion of therapeutic sera or of vaccines save the well-established procedure of vaccination against small-pox. Words and terms now in common use, as endocrines, vitamins, anaphylaxis, allergy, basal metabolism, hypertension, blood chemistry were unknown. Save perhaps in the brain of Roentgen himself, the x-ray was undreamed of. To the physician of that day the Wassermann test and salvarsan, antitoxin and amboceptor, radium and ultra-violet light, viosterol and salyrgan, renal lavage and type one pneumococcus serum would have been words and terms without relation to anything in the world. If by some legerdemain they could have been foretold, they would have been looked upon as coined for a medical "Alice in Wonderland."

The country doctor of that day knew that as the summer wore on and through the fall he would have typhoid to manage, often many such cases, always some. He knew that winter would bring diphtheria and scarlet fever, both prone to occur in epidemics, with high mortality rates and sequelae which shortened life. He knew that one aphorism of Hippocrates was still true, "The spasm that supervenes on a wound is fatal." Rarely did tetanus fail to kill. Cerebro-spinal meningitis, the dreaded "spotted fever," which now and then raged in epidemic form, took a toll of some eighty per cent in the death or disability of its victims. Tuberculosis, of which the common form was the pulmonary, commonly called "consumption," carried a sentence of death except to the favored few who could seek relief in a friendly climate. Many of these became permanent exiles.

Throughout the country generally public health activities were practically non-existent.

Not many years after my first acquaintance with "Osler" I used the third and fourth editions as text-books. A few years later I taught from one edition after another. In all, eleven editions have appeared, with only nine of which Sir William Osler was connected. Doctor Thomas McCrae, who assisted in the preparation of the seventh, eighth, and ninth editions, edited the tenth and eleventh. It is from the latter's preface to the ninth edition (written just after Osler's death) that I quote a sentence which may be offered as an excuse for this present venture in the realm of literature, "A study of successive editions represents a record of advance in medicine during a period of nearly thirty years." Now, through forty years, these eleven editions have taught beginners in medicine the accepted principles upon which practice is based. Osler has been accepted as a standard of "faith and practice." These years have seen more rapid increase of our knowledge and more radical changes in our conceptions of the nature and treatment of disease than any like period in history. With this has gone a change in the temper of the physician. Conservatism has given way to an openness of mind, which is sometimes too prone to embrace the new, an attitude like those of old who "spent their time but to hear or to tell some new thing." The public is so accustomed to the announcement of new remedies for disease that no small part of the physician's work is to admit his own inability to keep up with the latest medical discoveries as related in our daily papers.

Yet the first edition of Osler is not altogether obsolete. What we knew about small-pox, measles, chickenpox, and erysipelas forty years ago is about all that we know now. Trichinosis had been described by Zenker in 1860, and the article in the first edition is almost as illuminating as that in the last. While Osler was a student and throughout the early years of his career, the new science of bacteriology was rapidly developing in Germany, France, and England. His first edition includes descriptions of the fundamentals of bacteriology and its general relationship to the infectious diseases. The pathology of pulmonary disease, of cardiac and vascular disease, of hepatic and renal disease was taught in 1890 much as it is taught today.

Forty years ago typhoid fever was a major cause of disability and death. In most communities throughout the country the occurrence of typhoid was an annual event, beginning in early or mid-summer, reaching its peak in the early fall, and subsiding or dying out in winter. The general principles of the control of typhoid were obvious to the well-informed physician; the public was generally indifferent to the situation. As long ago as 1862, Murchison had written, "Instead of cutting off thousands annually, enteric fever would be a rare disease if we could prevent the products of fecal infection entering our houses and polluting our drinking water." Some twenty years after this was written the bacteriologist opened the way toward the realization of Murchison's ideal of prevention.

In his first edition Osler states that, "Eberth, Koch and Gaffky have shown that there is a specific micro-organism constantly associated with typhoid fever. . . . The poison is not given off from the skin or in the breath, but in the feces; the bacillus is found constantly in the intestines and is said to have been found rarely in the blood, in the rose-colored spots, and in the urine." He accepted the view that the infection occurs in water, and "infected milk is the result of the use of cans which have been washed with contaminated water." In his discussion of diagnosis, no laboratory procedures were mentioned except to note the absence of an increased white count and the value of blood examination in order to exclude the presence of malaria.

Three years later a larger number of possible sources of infection were specified. "Direct infection by dust of exposed food-stuff such as milk is very probable." In addition, we find mention of ice, salads, raw fruits and vegetables, "even cooked food may be readily contaminated by the soiled fingers of attendants." The following edition carried a description of the Widal test, recorded thus:

> "It was accordingly with great satisfaction that the announcement of a comparatively simple method of serum diagnosis was received. In 1894, Pfeiffer showed that cholera spirilla mixed with the serum of immunized animals lose their motion and break up.....This work determined the value of the test for the differentiation of bacterial species and for the determination of a previous attack of cholera or of typhoid fever and also that the immobilization and agglutination was a specific effect of infection or intoxication. Widal took the work and made it available for clinical purposes."

The same edition contained for the first time an italicized statement which is found through all the subsequent editions: "The physician should bear in mind the fact that each individual case of typhoid fever is a focus for the spread of the disease. To carry out effective measures of prophylaxis is as much a part of his duty as the care of the patient."

In the years which just preceded the publication of the fourth edition, the Spanish-American and the Boer wars had again emphasized the mortality from typhoid among soldiers in the field. "One fifth of the soldiers in the national encampments in the United States had typhoid fever. . . . In all modern campaigns it has usually appeared within two months and has proved the most fatal of camp diseases." Attention is also directed to the typhoid situation in Philadelphia which "gets its water from the Schuylkill and Delaware Rivers, the watersheds of which are populous with numerous towns. . . . In the autumn of 1898 there was a sudden increase in typhoid, and 1094 cases were reported in September due in part to the influx of soldiers with typhoid fever. The total number of cases for 1898 was 6,097 with 639 deaths; the total for 1899, 7,985 with 948 deaths." About this time the South African War was the scene of Sir Almroth E. Wright's attempt to immunize soldiers against typhoid by a "method of vaccination based upon the work of Haffkine in vaccinating against cholera." Osler believed that, "On the whole the experience so far is strongly in favor of inoculation."

In 1905 we read that in the United States census report for 1900 typhoid occupies the fourth place in the mortality list causing 35,379 deaths. Almost in the same sentence we are told of the results of proper preventive measures in the Japanese army then in the field against the Russians. In General Oku's army from May 6 to December 1, 1904, there were only 133 cases of typhoid fever and 342 of dysentery. The article on typhoid in this edition reports, "the value of the blood culture as a diagnostic procedure. This has been carried out extensively in my ward by Cole; I can testify to its great value in doubtful cases and in the acute septic forms." The same article includes the first reference to the persistence of the bacilli in the urinary tract of the recovered patient. "To stamp out typhoid fever requires, (1) the recognition of all cases and (2) the destruction of all typhoid bacilli as they leave the patient."

Before the outbreak of the Great War immunization against typhoid by means of vaccines was established. "Introduced by Wright, the method has proved of inestimable value in the United States Army, in India, and during the present war. . . . A triple vaccine against typhoid and paratyphoid A and B is now prepared and should be used. Untoward results are rare." Late editions have added little to methods of control or treatment of typhoid fever. The possibilities of preventive measures were so thoroughly demonstrated during the Great War that in recent years public sentiment has come to regard the presence

of typhoid as a reproach to a community, especially to officials charged with protection of the public health. Our larger cities are practically free from typhoid and the activities of State Health Boards have been effective in diminishing the incidence of the disease in rural districts.

"Diphtheria is a highly contagious disease, readily communicated from person to person. . . . It appeared early among the settlers of New England, and accounts are extant of epidemics in this country in the seventeenth and eighteenth centuries. . . . It is not confined to cities. It has prevailed with great severity in country districts, in which indeed the affection appears to be specially virulent. . . . No disease of temperate regions proves more fatal to physicians and nurses. . . . In country districts epidemics may display an appalling virulence and kill nearly all the children attacked. In cases of ordinary severity the outlook is good." These sentences are selected from the author's first description of diphtheria, about the treatment of which he concluded thus: "We are still without a remedy capable of combating in any way the effects of the poisonous toxalbumins."

The second edition reported the discovery of diphtheria antitoxin, the work of Behring and the earliest and one of the most effective of antitoxins. For this edition the section on diphtheria was rewritten. Already we find mention of healthy carriers, individuals in good health who harbor virulent bacteria in their throats. Following an attack of diphtheria virulent bacteria may persist in the throat after all signs of the disease have disappeared. Much of the success attained in the control of diphtheria is due to the efficient control of carriers. After quoting a report from the Boston City Hospital showing a reduction of the mortality from 44% to 25.9%, the author gives this guarded opinion, "A very much larger number of cases must be treated over a long period before final judgment can be reached." Meanwhile the antitoxin should be employed. The dosage recommended in those early days of serum therapy will bring a smile to physicians. In the third edition we read that, "Exceptional cases of great severity, especially when seen late, should receive somewhat larger doses than those mentioned—i. e., 3000 units. Mild cases should receive 1000 units for the first injection, a second being rarely required." The fourth edition quotes McCollom, "Who insists that the guiding practice in the use of the antitoxin is to give it until the characteristic effects are produced, whether 4000 or 70,000 units be required for this result." Present day methods of concentrating the serum have made larger doses easy to inject and unlikely to provoke reactions.

Those of us who remember the early days of the use of antitoxin, the bitter and often bigoted opposition offered by some physicians as well as laymen, will appreciate a quotation from the edition of 1901:

> "As the years go on, additional experience has shown that, thoroughly carried out, this method of treatment is both safe and efficacious. There are no reasonable grounds for scepticism on the part of intelligent practitioners, and still less on the part of those in charge of hospitals for infectious diseases. In this country, those in charge of institutions who still have any lingering doubts should, in the interests of their little patients, and in a spirit of humility, visit the South Department of the Boston City Hospital, and learn a few salutary lessons from its director, Dr. McCollom."

Though the work of producing an effective antitoxin for diphtheria was done, the general acceptance of the remedy was delayed, partly by prejudice, partly because of frequent serum reactions, which occasionally terminated fatally. It was soon established that these reactions were most violent in individuals subject to asthma, especially horse asthma. Incidentally, it may be remarked that much of our present knowledge of protein sensitization in asthma, hay fever, various skin lesions, and other diseases has developed from this by-product of the use of diphtheria antitoxin. The danger of serious results from

the antitoxin was minimized at first. In 1901, Osler stated in a short paragraph on "Untoward Effects," "Of these the most common are urticaria and arthralgia, but they are trifling and unimportant." It was not until 1909 that "serum sickness" was specifically considered; this reference includes the statement that sudden death has occurred in about twenty cases after the serum injection. The following edition contains a full description of serum disease and the methods of prevention and control, although the use of epinephrine is not mentioned until the eleventh edition. The work of Schick, who developed the toxin-antitoxin method of immunization was first described in 1920.

For many years, diphtheria antitoxin was unique; there existed no other antitoxic serum of established value. The preface to the seventh edition (1909) carries a reference to the "experiences of the last epidemic of cerebro-spinal fever in New York, Belfast, and Glasgow, with the hopeful work of Flexner at the Rockefeller Institute," and the text reports that, "A serum has been prepared and used with encouraging success." As early as the second edition reference had been made to tetanus antitoxin as prepared by Tizzoni and Cantani and by Behring and Roux. The value of these preparations was long in dispute. In 1901, our author admits that, "There may be occasion for the prophylactic use of the antitoxin in man, as already successfully practiced in arresting the spread of the disease in horses occupying infected stables." After a long period, prophylactic use in man of the anti-tetanic serum is recognized as an established procedure. Finally, in the tenth edition, the antitoxin is recommended in the treatment of the established disease. "Tetanus antitoxin should be given promptly and in sufficient dosage, the object being to saturate the patient as quickly as possible."

Referring in his first edition to the treatment for hydrophobia which Pasteur had presented, the author says, "There is still much discussion as to the full value of this method, but if the protective inoculation can be successfully performed in dogs, there is no reason why the same should not hold good for man." Six years later he recognized that discussion is not closed, "but the statistics published annually from the Pasteur Institute seem to prove conclusively its importance as a protective measure in man." In the next edition the sentence about the prevalence of discussion is omitted; evidently discussion as to the value of the Pasteur treatment is ended.

"As early as 1881 Finlay of Havana had suggested the possibility that the virus of yellow fever might be inoculated by the culex mosquito. In 1883 King, in the Popular Science Monthly, had proposed the same method of infection in malaria. In 1894 Sir Patrick Manson brought forward arguments in support of the conception that this insect might play the part of intermediate host of the malarial parasite."

Theobald Smith's studies of Texas Fever in cattle, published in 1893, stimulated interest in the subject of insect carriers of disease. A quotation from the section on malaria in the first edition is interesting in view of the light soon to be thrown upon the disease by the confirmation of the theory that mosquitoes are carriers of the infection.

> "The importance of the state of the soil in the etiology of malaria is universally recognized. It is seen particularly in low marshy regions which have an abundant vegetable growth. . . . Nothing can be truer than the fact that reeking marshes of the most pestilent appearance may be entirely devoid of the poison, and the disappearance of the disease from a locality is not necessarily associated with any material improvement in the condition of the marshes or of the soil. . . . . A tolerably high temperature is one of the essential conditions for the development of the virus. . . . . Many facts are on record which seem to indicate that the poison may be carried to some distance by winds. . . . . That the distribution of the poison of malaria is influenced by gravity has long been conceded. Persons dwelling in the upper stories or in buildings elevated some distance above the ground are exempt to a marked degree."

These observations were destined to be readily explained within a few years. The organism of malaria had been discovered by a French physician, Laveran, in 1880. The problems which still confronted the physician were summarized by Osler in a final sentence, "There are still many gaps in our knowledge. We do not know how the parasite enters, or how or in what form it leaves the body; how and where it is propagated; under what outside conditions it develops, whether free or in some aquatic plant or animal. No record of its successful cultivation has been published."

Nine years later most of these gaps in our knowledge had been closed. To quote again, "The brilliant researches of Ross, followed by the work of Grassi, Bastianelli, Bignami, Stephens, Christophers, and Daniels have proved that a certain genus of mosquito—anopheles—is not only the intermediate host of the malarial parasite, but also the sole source of infection. . . . So far as is known the parasite exists only in the mosquito and man." It was with enthusiasm over these advances that our author wrote: "In the discovery of Laveran there lay the promise of benefits more potent than any gift the laboratory had ever offered to mankind; viz., the possibility of the extermination of malaria. By the work of Manson, Ross, and others this promise has reached the stage of practical fulfillment, and one of the greatest scourges of the race is now at our command."

After eight years, we find facts presented which need no comment, "The story of the Canal Zone, Panama, under Colonel Gorgas is a triumph of the application of scientific methods. Between 1881 and 1904 among the employees of the French Canal Company the monthly mortality ranged from 60 to 80, once reaching the enormous figure of 177.97 per 1,000. In May, 1908, the mortality among 44,846 employees had fallen to the remarkably low figure of 10.44 per 1,000.

For generations the return of summer brought to the people in our southern states, especially the most southerly, the fear of yellow fever. In the early days of the Republic the disease prevailed as far north as Baltimore and Philadelphia.

> "The epidemic of 1793, so graphically described by Matthew Carey (of Philadelphia) was the most serious of any that had ever prevailed in any city of the middle states. The mortality as given by Carey during the months of August, September, October, and November was 4041, of whom 3425 died in the months of September and October. The population of the city at the time was only 40,000. . . . . In 1803 and 1805 it again appeared; then for many years the out-breaks were slight and localized. In 1853, the disease raged throughout the southern states. . . .In 1867 and 1873 there were moderately severe epidemics. In 1878 the last extensive epidemic occurred, chiefly in Alabama, Louisiana and Mississippi. The total mortality was nearly 16,000."

The last outbreak recorded was local, occurring in 1903, remaining confined to the immediate neighborhood of Laredo, Texas. The epidemic had started on the Mexican Border, and Osler points out the efficient work of our own public service as "shown by the differences between New Laredo on the Mexican border, just across the river, where 50% of the population contracted the disease, and Laredo, Texas, in which only 10% of a population of 10,000 were attacked."

In his fourth edition, published in 1901, Osler tells the story of the conquest of yellow fever. The American Commission on Yellow Fever, made up of Walter Reed, Carroll, Lazear, and Agramonte, under the direction of the Army

> "has demonstrated conclusively that yellow fever may be transferred by the mosquito culex fasciatus previously fed on the blood of infected persons. Non-immunes were kept under the most rigid quarantine, for a period, outside the endemic area, and then exposed in a specially constructed house to the bites of mosquitoes that had previously bitten cases of yellow fever. The experiment fulfilled the most exacting conditions of scientific accuracy, and forms a model of its kind. It was also shown that in non-immunes the disease would be produced by the subcutaneous or the intravenous injection of blood taken from patients suffering with the disease."

At Camp Lazear,

> "Dr. R. P. Cooke and two non-immune privates entered a house so constructed as to shut out sunlight and fresh air. The vestibule was thoroughly screened. The average temperature for 63 days was kept about 76 Fahrenheit. Boxes filled with sheets, pillow slips, blankets, etc., contaminated by contact with cases of yellow fever and the discharges, were placed in the house. For twenty days the three men occupied the room, each morning packing the infected articles in the boxes and at night unpacking them. In their experiments with the fomites, in all, seven non-immune subjects during a period of sixty-three days lived in contact with the fomites and remained perfectly well. These experiments, conducted in the most rigid and scientific manner, go far to discredit the belief in the transmission of the disease by fomites."

Experimentation in the production of yellow fever was possible only upon human beings. "In its graver forms yellow fever is one of the most fatal of epidemic diseases. The mortality has ranged, in various epidemics, from 15% to 85%." Osler closes his story of these experiments on volunteers in these words:

> "We must bear testimony to the heroism of the young soldiers who voluntarily, without any compensation, and purely in the interests of humanity submitted to the experiments, and also to the zeal and devotion with which members of our profession have, at the greatest possible risks, attempted to solve the riddle of this most serious disease. The death from the disease of Doctor Lazear of the American Commission and of Doctor Myers of the Liverpool Commission, adds two more names to the already long roll of martyrs of science."

"Typhus fever has been one of the great epidemics of the world. As Hirsch remarks, 'The history of typhus is written in those dark pages of the world's story which tell of the grievous visitations of mankind by war, famine, and misery of every kind. . . . .The history of typhus is that of human misery.' " Osler continues, "Typhus is one of the most highly contagious of febrile affections. In epidemics, nurses and doctors in attendance are almost invariably attacked. There is no disease which has had as many victims in the profession." Among the nations of the Western World, typhus has become almost obsolete, yet it still exists in the four corners of our world. In such a review as this we may not omit mention of a disease to the knowledge of which so much was contributed by two Chicago physicians. In the pursuit of these investigations H. T. Ricketts lost his life. Some thirty years ago, almost to the day, I heard Dr. Ricketts describe the results of his work on Rocky Mountain Spotted Fever. This was at the first meeting of the Chicago Medical Society I had ever attended. For years the existence of Mountain Fever, as an entity, had been in dispute. In his sixth edition, Osler had written, "It would be well for the use of the term mountain fever to be discontinued." Already Ricketts had identified the carrier as a tick which transmitted the parasite from animals to man, and this achievement Osler acknowledged in his next edition.

Subsequent to his successful studies of Rocky Mountain Fever, Ricketts, in association with Wilder, turned his attention to typhus fever. The eighth edition of Osler carries this sentence, "The typhus fever prevailing in Mexico City, where it is known as tabardillo, is more severe and, in its study, Ricketts, of Chicago, fell a victim." But not until he had made it possible for the author to continue, "The disease is transmitted by the body louse and possibly the head louse, and so is associated with filth and over-crowding." Ricketts had discovered an organism, probably the specific germ. The last edition states that, "The work of the Red Cross Commission strongly supports the view that *Rickettsia prowazeki* is the causal organism."

Since the days of Paracelsus, mercury has been used for the treatment of syphilis. In Osler's first edition the paragraphs on the treatment of syphilis were essentially a re-statement of opinions which had prevailed for decades. "The treatment of the disease is now practically narrowed to the use of two

remedies, justly termed specifics; namely, mercury and iodide of potassium. The former is of special service in the secondary, the latter in the tertiary manifestations of the disease; but they are often combined with advantage."

As late as the sixth edition, the author states that the nature of the virus is still doubtful, but the seventh edition appearing in 1909 tells a different tale:

> "Since the sixth edition of this work appeared there have been remarkable advances in our knowledge of syphilis—the discovery of the germ, the transmission of the disease to apes, and the serum diagnosis of the disease. The *spirochaeta pallida* discovered by Schaudinn, is found in primary, secondary, and tertiary lesions, and may be inoculated successfully into apes, monkeys, and rabbits . . . . Wassermann's reaction has reached the clinical stage and in good hands may be accepted as a valuable aid in diagnosis."

The next edition recorded further advance: "In 1910 Ehrlich announced the discovery of a compound which would destroy the parasite and not damage the individual." In the years since this appeared the arsenical preparations have been modified, the danger of reactions has been minimized, the bismuth preparations have been added. Though the treatment of syphilis is not yet perfected the treatment is now much more successful than it was fifteen years ago. Tryparsamide, an allied drug, has proved of value in the treatment of one type of the deadly African sleeping sickness.

In the first edition, after characterizing tuberculosis as one of the most widespread of maladies, reference is made to the work of Koch in these words, "It forms one of the most masterly demonstrations of modern medicine. Its thoroughness appears in the fact that in the nine years which have elapsed since its announcement the innumerable workers on the subject have not, so far as I know, added a solitary essential fact to those presented by Koch." The importance of early diagnosis is stressed; the gravity of the outlook for the patient in those early years of our knowledge of the nature of the disease is vividly expressed in the paragraph on prognosis, "In pulmonary cases the duration is extremely variable. Laennec placed the average duration at two years, and for the majority of cases, this is perhaps a correct estimate." The first edition states that the destruction of the sputum should be a routine requirement in hospital and private practice. In actual practice this was far from common at that time.

The need for institutional care was beginning to be appreciated:

> "The large cities should build special institutions within easy access by railway, with pleasant surroundings, in which early cases of pulmonary tuberculosis could be systematically treated. Advanced cases should not be admitted but should be cared for in separate wards of the city hospitals. Sanitaria for the care of recent pulmonary tuberculosis among the well-to-do classes are also urgently needed."

Nine years later progress is reported:

> "Perhaps the most important advance in the treatment of tuberculosis has been in the establishment in favorable localities of institutions in which patients are made to live according to strict rules. . . . . In this country the zeal, energy, and scientific devotion of Edward L. Trudeau have demonstrated its feasibility and the Saranac institution has become a model of its kind. We need public sanatoria within easy access of the large cities, in which cases of early tuberculosis could be treated at low rates or at the public cost."

The record of the great epidemic which prevailed in the reign of Justinian is probably the first of the disease known as the plague. The epidemics that raged throughout Europe in the fourteenth century are believed to have killed a fourth of the population. That the plague was an ever-present menace may be gathered from the stories of the small epidemics which infested London about the time that Charles I and his commoners began their quarrels; the latter complained bitterly of the call to London while the plague raged. The epidemic of 1665-1666 in London caused the death of 70,000 persons. Yet there is no mention of the plague in the first edition of Osler. The second edition contains

a description which barely fills a single page. It is noteworthy for this sentence, "A short but severe epidemic in May, 1894, at Hong Kong was rendered memorable by the discovery of the bacillus." The Japanese scientist, Kitasato, isolated the organism. In the next edition mention is made of Haffkine's method of preventive inoculation. In the fourth edition attention is directed to "the revival of the plague within the past ten years, which has aroused universal interest. Since the outbreak at Hong Kong the disease has appeared in many parts of the world." A few years later it is recorded that rats are subject to the disease and may be responsible (are often so) for outbreaks of plague. The author quotes Thompson of Sydney:

> "During an epidemic the only procedure of much value is destruction of rats and of their nests, burrows, and habitual haunts and those others which are calculated to prevent access of surviving rats to proximity with human beings. A general slaughter of rats would answer the purpose if it could be carried out quickly and with tolerable completeness . . . . The immunity of the human population seems to be due to the fact that 50% of one variety of rat fleas bite man, and the other rat flea does not bite man freely."

In the last edition the menace of the plague is thus referred to:

> "The revival of the plague is the most important single fact in modern epidemiology. Throughout the nineteenth century, it waned progressively. . . . . we had begun to put it with the sweating sickness among the diseases of the past. We knew that it slumbered in parts of China and in northwest India but the outbreak in 1894 at Hong-Kong showed that the 'black death' was still virulent. Since then it has spread in an ominous manner over many parts of the world. . . . . There have been small outbreaks in the United States at intervals from 1907 to the present with infection of rats and ground squirrels. The distribution in India is chiefly in the Punjab, Bombay, and the United Provinces, which have a combined population of about one hundred millions. In these provinces, between 1896 and 1911 about five and one-half million deaths occurred from plague. . . . . The Manchurian outbreak in the winter of 1910-11 was one of the most virulent on record, carrying off more than 45,000 persons in a few months."

Through nine editions the teaching about scarlet fever remained essentially unchanged. The second edition stated flatly that "the specific germ is not known." The same sentence is found in the ninth edition. The second edition tells us that, "It has even been urged that the disease is only a form of streptococcus infection." The ninth edition conveys the scepticism of the second: "The relation of the streptococcus is under discussion and the trend of work indicates that it is only a secondary invader and that there is not a specific streptococcus, though some have gone so far as to use streptococcic immunization as a prophylactic." The tenth edition announces the consummation of brilliant work: "The isolation of the strains of streptococci; the production of scarlet fever experimentally in human subjects, and the preparation of an antitoxin (by injection of the toxin into the horse) by G. F. and G. H. Dick are outstanding achievements."

I find in my notes a quotation for which I cannot give proper credit; nevertheless I make bold to use it; it expresses so much pertinent to this paper:

> "While the incidence of infectious diseases has been lessened, while some have been stamped out and others brought under control of prophylactic and therapeutic procedures, the practice of medicine is still engaged, to a large extent, in the care and prevention of disease due to minute organisms. Nature or Providence still provides work for the physician, and though he may be unpaid, he is not unemployed. New diseases have been discovered (not invented), and old diseases have been carried from parts of the world to which they had long been confined, to other parts, appearing as new diseases, providing work for the physician, the bacteriologist, and the sanitarian."

In the first edition, Osler described Malta Fever, which "prevails in the island of Malta and also in Naples and other districts of the Mediterranean." The disease rarely kills but is painful and capable of causing prolonged disability. "An English army surgeon described the presence of a micrococcus and this has been fully confirmed." In 1898, it is recorded, that "Hughes sug-

gests that some of the indefinite forms of fever in America conform to this type, but the evidence before us is certainly against this view.'' Three years later we learn that Malta Fever has been met with in India and China and occurs in Porto Rico and Manila. After six years we read that ''Only imported cases have been recognized in the United States.'' The next edition tells of the discovery of Zamit that, ''goats, the most important animals in the domestic life of Malta, were largely infected, from ten to fifteen percent having the organism in their milk.'' The edition of 1916 states that in the goat raising sections of Texas the disease is endemic.'' Finally, in the last edition, we find the old name supplanted by the new term ''undulant fever,'' and we are further informed that, ''A considerable number of cases has been reported in North America and Great Britain.'' One may well wonder how long cases of Malta Fever occurred in our country, overlooked as aberrant typhoid, or rheumatism, or unknown infection.

In the first edition there is a paragraph under the heading ''anchylostomiasis'' which reads thus:

> **"The existence of a parasite has long been known, but it was not thought to be pathogenic until Griesinger demonstrated its association with the Egyptian chlorosis. It has also been shown to be the cause of the anemia to which miners and brick-layers are subject. Throughout Europe the disease has been widely spread by the employment of Italian and Polish laborers. In certain Italian provinces it is extremely prevalent and serious. It occurs in India and Brazil and has been described in Jamaica. Dolley states that the parasite was described many years ago by physicians in the southern states, but no recent observations upon the disease have been made in this country."**

The same paragraph was carried in the second and third editions. In 1901, however, we find the statement that, ''Allyn has collected seven cases reported from the United States, in several of which the infection probably came through association with foreigners who brought the parasite with them to this country.'' The next edition which appeared within a year carried this startling statement, ''Stiles has shown that the disease prevails widely throughout the southern states, and is the chief cause of the anemia and poor health so common in many districts.'' Three years later progress is reported, ''In 1902, Stiles took up the study of the problem and demonstrated to the astonishment of the profession that the disease was endemic in many places and was the cause of the common anemia of the southern states.'' The subject was quite exhaustively treated in this edition. The interesting and ingenious theory of Looss, regarding the mode of infection, is worth quoting, ''The embryo worms readily enter the skin (of bare feet) and are carried by the veins to the right side of the heart and to the lungs. Escaping from the pulmonary vessels into the air spaces, they pass up the bronchi and the trachea to the pharynx and so down the gullet to the stomach and intestines.'' These remarkable observations of Looss have been confirmed by C. A. Smith's work. He has shown that it takes about seven weeks before the ova appear in the stools, and in the process of infection there may be sore throat and fever. It would appear that the skin is the common channel of entrance and usually shows signs of irritation known as ''Ground itch.''

In 1916 Stiles is again quoted in confirmation of the widespread incidence of the disease: ''The southern United States are badly infected. More than 12% of cotton mill employees are infected and the examination of recruits, college students, and school children in different parts of the country gives a percentage of infection of from 20 to 70 or 80%.'' The last edition mentions the extensive work of the Porto Rico commission and the International Health Board of the Rockefeller Foundation. In Porto Rico more than 300,000 people have received specific treatment for the disease.

Deficiency diseases are first indexed in the edition of 1920. Prior to this

time, pellagra was consistently classified as an intoxication and rickets as a constitutional disease, while beriberi was now an infection, now an intoxication, and scurvy, although long known to be prevented or cured by certain fruits or vegetables, was classified as a constitutional disease or a blood dyscrasia. Even yet, pernicious anemia is discussed under the general heading of diseases of the blood.

In the first edition pellagra is defined as ''a nutritional disturbance due to the use of altered maize. The disease occurs extensively in parts of Italy, in the south of France, and in Spain. It has not been observed in this country.'' It was probably endemic in Spain as long ago as 1735 and was described by an Italian, Frapolli, in 1771, who gave it the name, which means rough skin. A short description of the disease was essentially unchanged through six editions. In 1909, we find the statement that ''Searcy, Babcock, Wood, and Bellamy have shown (in 1907-1908) that it is not an uncommon disease in the southern parts of the United States; many of the cases are acute.'' The disease was still regarded as due to ''altered maize'' and the important preventive measure provision for ''proper ripening and preservation of the corn.'' The next edition contains a long discussion of recent studies. ''There are two main views, one that it is a deficiency disease, and the other that it is due to infection of some kind. . . . Experimental work suggests that it is a deficiency disease which may possibly be eradicated by a proper protein diet.'' The last edition continues equivocal: ''Diet plays the most important role in the causation, perhaps partly in the food balance, and also in the lack of a pellagra preventive factor for which the name vitamin G has been suggested. The exact combination or combinations is not clear. Yeast contains the largest amount of the preventive factor so far as known at present.''

The radical change in the treatment and prognosis of pernicious anemia is one of the triumphs of experimental medicine. For years regarded as a hopeless disease, treated in vain by all manner of methods, there came in 1926 the announcement of the promise of liver therapy. The performance has exceeded the most sanguine expectations. In the original edition the author defines the disease thus: ''There remains a group which, in the words of Addison, is characterized by a general anemia occurring without any discoverable cause whatever, cases in which there had been no previous loss of blood, no exhausting diarrhea, no chlorosis, no purpura, no renal, splenic, miasmatic, glandular, strumous, or malignant disease.'' In the paragraph on prognosis in which he includes the anemia of pregnancy, he writes, ''I know of no instance in a male in which the recovery has lasted for five years.'' Thirty-three years later, pernicious anemia is defined as, ''a recurring and usually fatal anemia caused by hemolytic agents and characterized by an embryonic hematopoiesis. . . . . The cause remains obscure, the nature and origin of the hemolysin are unknown. . . . . The ultimate prognosis in a great majority of cases is bad; only one case in our series appears to have recovered completely.''

How different the paragraph on prognosis found in the last edition. ''The introduction of liver therapy has completely altered the prognosis; and gives the hope that the great majority of patients can look forward to a great prolongation of life. It is essential that the liver therapy be continued permanently in the necessary amount.''

In the first edition, the article on exophthalmic goiter presents views on pathogenesis far removed from present doctrines. In the section on morbid anatomy no suggestion is made that the enlarged thyroid is primarily responsible for the disease.

"No constant changes have been found in exophthalmic goiter. Special attention has been paid to the condition of the sympathetic system, as the rapid action of the heart and dilatation of the vessels have been attributed to paralysis of the sympathetic fibers, particularly the vaso-dilators. This view has found many supporters, but neither in the ganglia nor in the nerves are there any changes which can be regarded as constant and peculiar. On the other hand, many features of the disease are explicable on the view that it is an affection of the medulla oblongata, and Hale White has reported a case dying of an acute intercurrent disease in which there were hemorrhages in the floor of the fourth ventricle. The vascular and nervous features might be due to a lesion of this part; but it is difficult on any theory to explain all the symptoms of the disease and to bring into line the mental and vascular phenomena, the exophthalmos, and the goiter."

The author is pessimistic about the prognosis.

"The course of the disease is chronic, lasting several years. . . . . A certain proportion of cases recover, but when the disease is well-developed recovery is rare. . . . . Treatment of the thyroid gland itself is rareful successful, and the operative measures have not been very satisfactory."

In the next edition, modern views are forecast:

"Of late years, the view has been urged, particularly by Moebius and Greenfield, that exophthalmic goiter is primarily a disease of the thyroid gland (hyperthyrea) in antithesis to myxoedema (athyrea). . . . . Greenfield has shown that thyroid extract given in excess produces symptoms not unlike those of Basedow's disease—tachycardia, tremor, headache, sweating, and prostration. . . . . Use of the thyroid extract usually aggravates the symptoms of exophthalmic goiter."

The third edition evaluates the early surgery of the thyroid:

"Operative measures seem to offer the greatest relief. Removal of one lobe of the gland, tying the arteries of the gland, and exothyroplexia all have been tried. The patients, as a rule, stand the anaesthetic badly; death on the table is more frequent than published records indicate."

Eight years later the author is more hopeful of surgery, "Removal of part of the thyroid gland offers the best hope of permanent cure. It is remarkable with what rapidity all the symptoms may disappear after partial thyroidectomy." In recent years increased precision of diagnosis and more efficient pre-operative care based upon the clinical determination of the basal metabolism and Plummer's epochal announcement of the value of Lugol's solution in the preparation of the patient for operation have given confidence to the operator. Relief, with a minimum of risk, is now the privilege of most of the sufferers from hyperthyroidism.

I cannot forbear to quote from two of the earlier sections on myxoedema. In the first edition the hopelessness of the condition is described thus:

"Unfortunately no satisfactory treatment is known. The patients suffer in cold and improve greatly in warm weather. They should, therefore, be kept at an even temperature, and should, if possible, move to a warm climate during the winter months."

Three years later came an outburst of enthusiasm:

"Our art has made no more brilliant advance than in the cure of those disorders due to disturbed function of the thyroid gland. That we can today rescue children otherwise doomed to hopeless idiocy—that we can restore to life the hopeless victims of myxoedema is a triumph of experimental medicine for which we are indebted very largely to Victor Horsley and his pupil Murray. . . . . We now know that the gland, taken either fresh, or as the watery or glycerin extract or dried, is equally efficacious in a majority of the cases of myxoedema in infants or adults."

Though it took many years to utilize a product of the pancreas for the control of diabetes, the relationship between pancreatic disease and diabetes was considered some years before Osler's book was published. The first edition contains reference to this work. "Interesting observations have of late made it probable that the pancreas may in some cases be the seat of the trouble. . . . . The pancreas is believed to have a double secretion, external and internal; the latter passes into the blood and is supposed to be of the nature of a ferment, in the presence of which alone, the normal assimilative processes can take place

with the glycogen. Disease of the pancreas causes diabetes by preventing the formation of this sugar-splitting ferment." Progress in knowledge of physiology had not yet modified the prognosis, the paragraph on which contains this passage,

"Personally I have never seen recovery from a true diabetes. Temporary arrest, reduction to a minimum of the amount of sugar excreted, and prolonged periods of good health, I have frequently seen, but neither in any one of my personal friends or acquaintances, who have suffered with the disease, nor in patients, who have come under my care in hospital or private practice, have I known permanent and complete disappearance of the sugar so that an ordinary diet could be taken with impunity. . . . . Our injunctions today are those of Sydenham; 'Let the patient eat food of easy digestion, such as veal, mutton, and the like, and abstain from all sorts of fruits and garden stuff."

The second edition presented more proof of the relationship of the pancreas to diabetes, including incidentally, a statement that, "A patient of W. T. Bull died of diabetes after extirpation of the pancreas." In the fourth edition we find added evidence including reference to the observations of Opie from Doctor Welch's laboratory, "Imbedded in the pancreas are the peculiar bodies known as the islands of Langerhans." These islands are in reality ductless glands like the parathyroid, the thyroid, and the pituitary.

But no measures to control the disease with any degree of satisfaction were devised. The young diabetic faced an early death, usually in coma. Occasionally patients might be restored to consciousness for a few hours. None recovered. Elderly diabetics were not so quick to develop coma, but diabetic gangrene took its toll, intercurrent diseases, especially infections were often fatal, diabetic neuritis with its terrible punishment of the patient was not uncommon; carbuncles were common and often fatal, and the diabetic who needed any operation requiring a general anesthetic faced a tremendous risk; the mortality under such circumstances was high. The succinct prognosis of Saundby was all too true, "Life seemed to hang by a thread, a thread often cut by some trifling accident."

In 1916 the starvation treatment of Allen was proposed and eagerly accepted; accepted by the profession but not by the patients. Though the method doubtless did prolong life for many who were amenable to such discipline the majority of diabetics would not accept the rigid dietary reductions. Such was the situation when the discovery of insulin was announced in 1922. "The discovery of insulin by F. G. Banting working with C. H. Best and J. B. Collip, in association with J. R. Macleod, has revolutionized the treatment of diabetes."

Through forty years, following the changes in a standard textbook, which has enjoyed unusual favor, we have sketched a few of the more brilliant achievements in the warfare against disease. The catalogue of medical progress, since the advent of Osler as author, is far too long to permit of further reference to specific instances here. It would be difficult to cite a branch of internal medicine which has not been radically altered, in content and procedure, during the past four decades. Osler was quick to note the rapid changes. In the preface to the fourth edition we read that "many and important changes have been made in this edition." Five years later, in the sixth edition, it is noted that, "So many sections have been rewritten and so many alterations made that in many respects this is a new book." In 1912, the author returned to this subject in his preface, "In the twenty years that have passed since the publication of the first edition, triennial revisions have appeared regularly with one exception. . . . . comparing the first edition with the present, very little remains of the original work." It remains to consider briefly the sources of power which enabled Sir William Osler to exert so large an influence in the

promotion of modern medical knowledge, an influence which gave to him a position of leadership in his profession, so great, that it may be said without exaggeration, throughout the latter part of his life he was the best known and most highly regarded physician in all the world.

To what shall we attribute the success of this book? Was it good fortune, "luck" alone, or predominantly? Was it merely by chance that the author received instant recognition and his book such preference that through forty years it has been difficult for another text-book of medicine to find standing room? The Goddess of Fortune smiled indeed, not upon one who idly sought her favor, but upon a claimant who was richly prepared to bear well the honors heaped upon him and to justify their disposition. Osler was endowed with the personal characteristics and acquirements of the successful teacher. For his work as a teacher of medicine he had received a thorough training in the fundamentals of medical science, especially in morbid anatomy, which occupied an especially significant place in the teaching program of that day. To this he added an excellent training in clinical medicine. He had "walked the wards" with the leading teachers in European clinics. He had caught the spirit of his time, he had met many of the experimental investigators who were playing a large part in the development of bacteriology, experimental pathology, and medicine, and the application of chemistry and physics to medicine. Yet with his openmindedness to the new, his appreciation of the fact that scientific investigation was leading the medical profession to increased usefulness, he was never a scientist alone; Osler was a physician in all the word implies. His particular interest was in the diagnosis and treatment of disease; to him the purpose of medicine was attained in the cure or relief of the sick person. These qualities of mind and heart were united to a singular gift of expression, rarely eloquent, but almost invariably plain, direct, pertinent. The junior student in medicine understood his language, appreciated his illustrations, grasped his conclusions, and could, if he would, sense the purpose of the author to promote the welfare of his fellow-men.

It would not have been surprising if the timeliness and modernity of the first edition had been followed by the disposition to hasty acceptance of new views in medicine. Enthusiasm was "in the air." Instead, the author distinguished himself, as successive editions appeared, by a conservatism regarding new views of etiology and pathology, new methods of diagnosis, and new procedures in treatment. He was not quick "to lay the old aside." McCrae, in one of the later prefaces, quotes the senior author as having once replied to the complaint that he had not included certain new work in a recently published edition, "A text-book is not a year-book." He did not neglect his obligations to the general practitioner who looks to a text-book for a final statement as to current teaching and cannot submit to be disturbed and unsettled by theories still in process of experiment. At times, his attitude seems to have been very conservative. We have already quoted passages illustrative of his delay in accepting Pasteur's conclusions; he was slow, almost stubborn, in declining to follow, in the first decade of this century, the movement for more liberal diet in typhoid, and even in the latest editions the indications for appendicitis are not as dogmatically in favor of operation as to coincide with the views of many of us. Yet, this must be said, once a discovery or a new method of practice was accepted by the author and recommended to the profession, rarely did it happen that retraction was necessary. This acceptance might need qualifications upon the basis of further studies, but the underlying principle was not shaken.

In his essays and occasional addresses, our author made manifest his ability to write gracefully. His style is reminiscent of the first rate essayists of his time; informative, frequently charged with the moral fervor indicative of his allegiance to high ideals of medical practice, of which he was himself an outstanding example. In this branch of literature, he demonstrated the delicate precision and smoothness of the Greek; his text-book was of a different mold, disclosing the solid and matter-of-fact style of the Latin.

Osler's text-book is singularly clear and to the point. The student found it easy to remember what he had read by memorizing the headings of paragraphs; these were so aptly chosen and so fitted to the content of the paragraph. Not infrequently did it happen that one could easily recall the main features of a fairly long description of a particular disease if he had taken the pains to memorize the definition with which the section opened. Without pretense to the manner of literature the author developed a style which conveyed his thoughts to the student and the busy practitioner. His language carried to the reader such conviction of knowledge, experience and integrity that student and practitioner alike looked to him for final guidance through almost thirty years of his life. McCrae in the preface to the ninth edition, written just after the senior author's death, characterizes his style thus, "With the art of extracting and condensing the essentials of a subject went the ability to present them clearly. His use of the telling phrase often drove home a point more strongly than a long description could do."

The author chose two mottoes for his book, the second of which, from Plato's *Gorgias* runs thus, "And I said of medicine, that this is an art which considers the constitution of the patient and has principles of action and reasons in each case." May I close my essay with this simple comment, that if this be medicine, then medicine was personified in Osler.